

Serial No. 10/686,801

Docket No. 4822-129 US

Amendments to the Specification:

Please replace the paragraph beginning at page 5, line 1, with the following rewritten paragraph:

Chromium exists mostly in two valence states in nature, namely, hexavalent chromium [chromium(VI)] and trivalent chromium [chromium(III)]. Chromium(VI) is commonly used in industrial chrome plating, welding, painting, metal finishes, steel manufacturing, alloy, cast iron and wood treatment, and is a proven toxin, mutagen and carcinogen. The mechanistic cytotoxicity of chromium(VI) is not completely understood; however, many studies have demonstrated that chromium(VI) induces oxidative stress, DNA damage, apoptotic cell death and altered gene expression. Conversely, chromium(III) is essential for proper insulin function and is required for normal protein, fat and carbohydrate metabolism, and is acknowledged as a dietary supplement. Chromium(III), in absence of antioxidants, is converted to Chromium(VI) by spontaneous systematic oxidation hence it induces delayed toxicity. ~~This can be avoided using Chromium(III) complexed with an appropriate antioxidant ligand.~~ Comparative concentration- and time-dependent effects of chromium(VI) and chromium(III) have demonstrated an increased production of reactive oxygen species (ROS) and lipid peroxidation, enhanced excretion of urinary lipid metabolites, DNA fragmentation and apoptotic cell death in both in vitro and in vivo models. Chromium(VI) demonstrated significantly higher toxicity as compared with chromium(III). Chromium(VI) induced more pronounced oxidative damage in multiple target organs in p53 deficient mice.

At page 10, following the sub-heading "Selection of Phenolic Antioxidants" please add the following paragraph:

Chromium (III), in absence of antioxidants, is converted to Chromium (VI) by spontaneous systematic oxidation hence it induces delayed toxicity. This can be avoided using Chromium(III) complexed with an appropriate antioxidant-ligand.